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EXAMINER	
BARTON, JEFFREY THOMAS	

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,354	BOHM ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Barton	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-24 and 26-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-24 and 26-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20050616*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 June 2005 has been entered.

Response to Amendment

2. The amendment filed on 16 June 2005 and entered on 5 August 2005 does not place the application in condition for allowance.

Status of Objections and Rejections Pending Since the Office Action of 15 February 2005

3. The objections to claims 46-48 are withdrawn due to Applicant's amendment.

4. The rejection of Claim 20 under 35 U.S.C. §112(1) as failing to comply with the enablement requirement is withdrawn due to Applicant's amendment.

5. All other previous rejections are maintained.

Claim Rejections - 35 USC § 112

6. Claims 1-3, 5-24, and 26-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As currently amended, each claim has the limitation, "each of said fluid interface ports having . . . a diameter that is significantly larger than the depth so as to minimize a total volume of the fluid interface port". It is not clear how specifically having a port diameter *larger* than the depth helps to minimize the port volume.

Claim Rejections - 35 USC § 103

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 1, 2, 5-8, 30-37, 39-41, 43, 44, and 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al (WO 99/64850) in view of either McCormick et al or Amigo. Since WO 99/64850 is in German, citations below are given to US Patent No. 6,846,398, which issued from the National Stage entry of this International Application.

Relevant to claims 1 and 46-48, Heller et al disclose a separation device (Figures 1 and 2) comprising: anode and cathode reservoirs (P1 and P2); a plurality of channels connected to the anode reservoirs with each of the channels having an interior bounded by a side wall; a plurality of interface ports (A) formed in the sidewalls of the channels to

provide access to the channel, each of the ports having a depth equal to the sidewall (i.e. cover) thickness (Column 6, lines 1-2); with the anode and cathode reservoirs multiplexed with the channels. (Figure 1)

Relevant to claims 30 and 32, Heller et al disclose a separation device comprising: a substrate (Chip C; Column 4, lines 35-37); a plurality of channels formed in the substrate (Figures 1 and 2), each channel having an interior bound by a side wall; a plurality of interface ports (A) that provide access to the interiors of the channels (Figure 2; Column 6, lines 1-2); an anode reservoir multiplexed to two or more separation channels; and a cathode reservoir multiplexed to two or more separation channels (Reservoirs P1 and P2; Figure 1)

Relevant to claim 39, Heller et al disclose a method of injecting a liquid into their separation device, comprising: connecting a cathode reservoir to the respective first ends of two or more channels; connecting an anode reservoir to the respective second ends of these channels (Figure 1; Column 4, lines 27-31; construction of the device inherently includes steps as recited); forming a droplet of the sample and directing it through an interface port (Column 6, lines 20-28 and 50-52); and applying a voltage to the port in order to inject the sample into the channel. (Column 3, lines 30-32; the charged pin will inherently carry a voltage to the port in the injection step)

Relevant to claims 40 and 43, Heller et al disclose a method of forming a separation device comprising the steps of: forming a plurality of separation channels in the device, each channel being defined by an interior bounded by a side wall; forming a plurality of fluid interface ports (Figure 2, port A) leading to the channels; connecting an

anode reservoir to two or more channels; and connecting a cathode reservoir to two or more channels. (Column 4, lines 27-31; construction of the device inherently includes steps as recited)

Relevant to claims 2 and 34, Heller et al disclose an electrode array coupled or coupleable to the reservoirs and fluid inlets within the separation device. (Figure 1; Electrodes E1-E4)

Relevant to claim 6, Heller et al disclose such an array of apertures (Figures 1 and 2)

Relevant to claims 7, 31, 33, 41, and 44, Heller et al disclose channel widths of 20 - several hundred microns, and the port diameter is bounded by the channel width. (Figure 2; Column 4, lines 61-62; Column 5, lines 21-25)

Relevant to claim 8, Heller et al disclose their device being a capillary array electrophoresis plate. (Figure 1; Column 1, lines 5-10)

Relevant to claim 35, Heller et al disclose the regular spacing of the interface ports such that they can receive solutions from a parallel loading device. (Column 6, lines 20-28)

Relevant to claims 36 and 37, Heller et al disclose a parallel loading device comprising a multi-headed pipetter or pins for carrying droplets. (Column 6, lines 20-22)

Heller et al do not explicitly disclose the thickness of their cover, which is pertinent to the dimensional limitations of the instant claims, an interface port wider than it is deep, or a "virtual wall" meniscus.

McCormick et al disclose a microfluidic system similar in construction to that of Heller et al, in which they cover the channels with a cover as thin as 10 microns. (Column 13, lines 17-22)

Amigo discloses a microfluidic system similar in construction to that of Heller et al, in which they cover the channels with a cover as thin as 10 microns. (Column 8, lines 1-6)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device and methods of Heller et al by specifically using a cover as thin as 10 microns, as taught by either McCormick et al or Amigo, because the silence of Heller et al concerning this indicates that a skilled artisan could choose any suitable cover thickness such as those known in the prior art, e.g. McCormick et al or Amigo. The choice of thinner material could be motivated by reduction of material consumption, which could potentially reduce manufacturing costs.

Designation of a channel as a "separation" channel in structural limitations is not given undue weight in these rejections, as it points to an intended use of a device rather than defining a specific structure. Each section of "injection" channel associated with a particular "separation" channel in Heller et al is referred to as a separate channel, although all are joined. (Column 7, lines 6-12) However, some separation of charged components of different charge to mass ratios will inherently occur upon exposure to a

DC electric field, such as during the injection as described by Heller et al. Additionally, Heller et al disclose that sample migration in the "injection" channel beyond the intersection with the "separation" channel need not occur. (Column 5, lines 59-63) In effect, this results in the "separation" channel running from the injection port to the downstream reservoir, as the separation will commence upon the first exposure of the injected sample to an electric field. (i.e. between electrodes E3 and E4)

Regarding the independent claims, within this combination, with a channel and port width of twenty to hundreds of microns (Column 4, lines 61-62; Figure 2) and cover thickness of 10 microns, the limitation to a port diameter significantly larger than its depth is met.

Regarding the limitations to a "virtual wall" and port dead volume of less than a picoliter or zero, Heller et al provide no explicit disclosure except that all channels in their system are filled with a separation medium (Column 5, lines 66-67), and therefore a medium/air interface will exist at these ports. Whether the medium forms a meniscus at the interior or exterior surface of the port depends on the cross-sectional area of the port vs. that of the channel - fluid will naturally be drawn into the narrower opening, driven by its surface tension. While no explicit channel depth is recited by Heller, a shallow channel could obviously be used (e.g. about twice as wide as it is deep, as conventionally results from isotropic glass etching). An approximately hemicylindrical 100 micron wide, 50 micron deep channel would have a cross section of 1250π square microns, while the port configuration of Figure 2 of Heller et al for this channel would be a circle with 100 micron diameter, having a cross section twice as large. In the absence

of applied pressure, fluid in the channel would not be drawn into the port to a significant extent, and the meniscus would form at the bottom surface of the wall, leading to a port dead volume of substantially zero. Given a conventional flowable separation medium, this meniscus could only correspond to the instantly claimed "virtual wall", as no distinction between the respective ports, associated channels, or fluids can be seen.

Regarding claim 49, a meniscus that forms anywhere from the upper to lower surface of the interface port can be described as "coplanar" with the sidewall channel.

9. Claims 1-3, 5-8, 12-24, 26, 30-36, and 38-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al in view of Howitz et al.

Relevant to claim 1, Simpson et al disclose a separation device (Column 1, line 65 - Column 2, line 1) comprising: one or more anode reservoirs (Figure 1, 180; Column 9, lines 25-27)); a plurality of separation channels connected to the anode reservoirs (Column 3, lines 14-28; Column 9, lines 25-27), with each of the separation channels having an interior bounded by a side wall (Figure 4B; Column 4, line 47 - Column 5, line 7); a plurality of fluid inlets to the separation channels (Figure 2, B and C with associated channels to channel 222); and at least one cathode reservoir multiplexed with two or more separation channels. (Figure 1, Reservoir 120)

Relevant to claim 12, Simpson et al disclose a separation device comprising: an array of microfabricated separation channels formed at the surface of a first microfabricated substrate and a corresponding surface of a second substrate bonded to the surface of the first substrate with each channel having an interior bounded by a

sidewall, a first end and a second end (Figures 1 and 4B; Column 9, lines 12-17; Column 4, line 47 - Column 5, line 7); an array of fluid inlets to the separation channels (Figures 1 and 2, B and C with associated channels to channel 222); an array of cathode reservoirs connected to the first end of each of the separation channels (Figure 1; Column 9, lines 23-24); and an array of anode reservoirs, wherein at least one anode reservoir is connected to the respective second ends of at least two of the separation channels. (Figure 1; Column 9, lines 25-27)

Relevant to claims 30 and 32, Simpson et al disclose a separation device comprising: a substrate (Column 4, line 47 - Column 5, line 7); a plurality of separation channels formed in the substrate (Column 3, lines 14-28), each channel having an interior bound by a side wall (Figure 4B; Column 4, line 47 - Column 5, line 7); a plurality of fluid inlets to the separation channels (Figure 2, B and C with associated channels to channel 222); an anode reservoir multiplexed to two or more separation channels (Figure 1, Reservoir 180; Column 10, lines 49-57); and a cathode reservoir multiplexed to two or more separation channels (Figure 1, Reservoir 120; Column 10, lines 58-65)

Relevant to claims 2, 16, 17, 22, and 34, Simpson et al disclose an electrode array coupled or coupleable to the reservoirs and fluid inlets within the separation device. (Column 5, line 36 - Column 6, line 37; Column 10, lines 9-10) This array can be in electrical contact with the device (Figure 4B; Column 10, lines 31-33), or integral with the substrates of the device (Column 10, lines 11-13).

Relevant to claim 3, Simpson et al disclose a separation device with an outer perimeter and a center, with the separation channels connecting the outer perimeter to the center. (Figure 9; Column 9, lines 9-11)

Relevant to claims 8 and 26, Simpson et al disclose their device being a capillary array electrophoresis plate. (Column 1, lines 65-66)

Relevant to claim 14, Simpson et al disclose the first and second substrates being made of glass. (Column 9, lines 66-67)

Relevant to claim 15, Simpson et al disclose the first and second substrates being made of plastic. (Column 10, lines 1-2)

Relevant to claims 18 and 35, Simpson et al disclose the regular spacing of the fluid inlets on one of the substrates to receive solutions from a parallel loading device. (Column 1, lines 13-15; Column 4, line 47 - Column 5, line 7)

Relevant to claims 19 and 24, Simpson et al disclose the first substrate of their device including an array of electrodes aligned with sample reservoirs of the device to make electrical contact with solutions in the sample, waste, anode, and cathode reservoirs. (Column 10, lines 17-23)

Relevant to claim 20, Simpson et al disclose a number of holes, H, approximately equal to 5N/4, where N is the number of samples to be processed. (Column 10, lines 24-27)

Relevant to claim 21, Simpson et al disclose their device being made of a combination of glass and plastic. (Column 10, lines 28-30)

Relevant to claim 23, Simpson et al disclose a plurality of sample fluid inlets in communication with on of the separation channels (e.g. Figure 2, B and C both feed channel 222)

Relevant to claim 36, Simpson et al disclose a parallel loading device comprising a multi-headed pipetter. (Column 11, lines 16-18)

Relevant to claim 38, Simpson et al disclose the disposition of the separation channels in a radial pattern on the separation device. (Figure 9)

Relevant to claim 39, Simpson et al disclose a method of injecting a liquid into their separation device, comprising: connecting a cathode reservoir to the respective first ends of two or more channels (Column 11, lines 29-30); connecting an anode reservoir to the respective second ends of these channels (Column 11, lines 31-32); loading a sample liquid into the sample reservoir; and applying a voltage to inject the sample into the separation channel. (Column 8, lines 32-41; Column 11, lines 33-41)

Relevant to claims 40 and 43, Simpson et al disclose a method of forming a separation device comprising the steps of: forming a plurality of separation channels in the device (Column 11, line 49), each channel being defined by an interior bounded by a side wall (Figure 4B; Column 4, line 47 - Column 5, line 7); forming a plurality of sample reservoirs connected to the channels (Column 11, lines 50-54); connecting an anode reservoir to two or more channels (Column 11, lines 55-56); and connecting a cathode reservoir to two or more channels. (Column 11, lines 66-67)

Relevant to claims 42 and 45, Simpson et al disclose the radial disposition of the channels on the separation device. (Figure 9)

Simpson et al do not explicitly disclose a device comprising: fluid interface ports formed in the side walls of the separation channels to provide access to the interiors of the separation channels, wherein the diameter of the port is significantly larger than its depth, wherein a separation medium disposed in the interior of the separation channel forms a virtual wall at each fluid interface port, and wherein each fluid interface port has a dead volume less than about 1 pL (Claim 1), zero dead volume (Claim 5), or diameters between 25 and 125 μm. (Claims 7, 13, 25, 31, 33) They also do not explicitly disclose a fluid interface port that comprises an array of apertures forming virtual walls. (Claim 6)

Regarding claim 39, Simpson et al do not explicitly disclose forming a droplet from the liquid sample, or directing the droplet to a virtual wall formed by a separation medium in a fluid interface port formed in the sidewall of a separation channel.

Regarding claims 40-45, they also do not explicitly disclose a method comprising forming the plurality of ports in the channel sidewalls by removing portions of the sidewalls to define ports with diameters between 25 and 125 μm.

Howitz et al disclose a device (Figure) comprising: fluid interface ports (capillaries containing menisci 6) formed in the side wall of a fluid channel (9) to provide access to the interior of the fluid channel, wherein a separation medium disposed in the interior of the fluid channel forms a virtual wall at each fluid interface port (Menisci 6).

(Column 3, lines 11-15) Relevant to claim 6, they also disclose a fluid interface port comprising an array of apertures forming virtual walls.

Relevant to claim 39, Howitz et al disclose a method of sample injection comprising: forming a droplet from the liquid sample (Figure, droplet 5; Column 3, lines 31-34), and directing the droplet to a virtual wall formed by a liquid in a fluid interface port formed in the side wall of a flow channel.

Relevant to claims 40-45, they also disclose a method of forming their fluid interface ports, comprising the step of forming fluid interface ports in the channel sidewalls with diameter between 25 and 125 μm. (Column 3, lines 12-15, length and width are 50 μm)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Simpson et al by replacing the sample and waste reservoirs, and their associated side channels with a simple hole or holes through the sidewall to serve as a fluid port, as taught by Howitz et al, because Howitz et al teach the usefulness of their fluid port in introducing fluids to microchannels while preventing outflow of the fluid contained within the channel. (Column 1, lines 53-58) It would also reduce the number of holes required in the device by eliminating the need for injection crosses, this reduction in the number of holes having been taught by Simpson et al to be desirable. (Column 3, lines 50-65)

Further addressing claims 1 and 5, given the definition of dead volume presented in the instant specification (roughly, the volume of liquid held in the port and not flowing

with the fluid within the channel), the dead volume associated with ports such as those of Howitz et al will be variable, as a function of the affinities of the fluids for the surface of the port, among other factors. (Column 3, lines 25-31) As such, the dead volume will be zero or near zero (i.e. less than 1 picoliter) for a clean hydrophobic port surface in a device using aqueous fluids. Such hydrophobicity is an innate property of many polymers known to be useful in manufacturing microfluidic devices (e.g. fluoropolymers) or it could be achieved by using known surface treatments for glass (hexamethyldisilazane, used by Simpson - Column 4, lines 53-56) and silicon (Hydrofluoric acid), and would constitute an obvious modification of the device, because such a surface would minimize loss of the injected sample. (i.e. if an aqueous sample hit a hydrophobic surface in a port configured in the way shown in the Figure of Howitz et al, substantially the entire droplet would immediately fall into contact with the fluid in channel 9, as the contact angle and reduced frictional force would not be sufficient to retain the droplet on this surface)

Regarding the limitation that the port be wider than it is deep, although the example given by Howitz et al does not meet this limitation, Howitz et al also disclose variation of the depth of the port. (i.e. length of the capillary; Column 2, lines 5-10 and 27-30) Choice of a shorter length such that this limitation is met would have been obvious to a skilled artisan, particularly given the trend towards miniaturization in this art.

Further addressing claim 20, by replacing each sample reservoir with a fluid interface port, and eliminating waste reservoirs, the number of holes in this combination

device would be reduced to N+A+C, where N is the number of samples to be analyzed, A is the number of anode reservoirs, and C is the number of cathode reservoirs.

Regarding claim 39, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Simpson et al by altering the injection step by: forming a droplet of the sample and directing it to the virtual wall formed at a fluid interface port by a liquid in the separation channel (in the combination device of Simpson et al and Howitz et al described above), as taught by Howitz et al, because it would reduce waste of the sample liquid.

Regarding claims 40-45, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Simpson et al by replacing the step of forming sample reservoirs and associated side channels with the formation of a simple hole or holes (50 μm length and width) through the sidewall to serve as a fluid port, as taught by Howitz et al, because Howitz et al teach the usefulness of their fluid port in introducing fluids to microchannels while preventing outflow of the fluid contained within the channel. It would also reduce the number of holes required in the device by eliminating the need for injection crosses, this reduction in the number of holes having been taught by Simpson et al to be desirable. (Column 3, lines 50-65)

Regarding claims 46-48, each of these claims fully encompasses claim 1 in that they only recite limitations that are present in claim 1, while removing various other limitations. The prior art as applied to claim 1 above therefore also renders these claims obvious, given their open language (i.e. "comprising").

Regarding claim 49, a meniscus that forms anywhere from the upper to lower surface of the interface port can be described as "coplanar" with the sidewall channel.

10. Claims 9-11 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al and Howitz et al as applied to claims 1 and 12 above, and further in view of Bjornson et al.

Simpson et al and Howitz et al disclose combinations as described above in addressing claims 1 and 12.

Neither Simpson et al nor Howitz et al disclose their devices being used for electrochromatography (Claims 9 and 27), pressure-driven chromatography (Claims 10 and 28), or isoelectric focusing (Claims 11 and 29).

Bjornson et al disclose electrophoretic devices used for isoelectric focusing and capillary chromatography. (Column 12, lines 53-59) They also disclose fluid flow in their devices by electroosmosis (Column 11, lines 55-60), which suggests electrochromatography. (i.e. chromatography in which the motion of the mobile phase is caused by an electric field)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Simpson et al and Howitz et al by providing the separation capillaries with a chromatographic medium, immobilized pH gradient, or ampholytes and using the device for electrochromatography or isoelectric focusing, as taught by Bjornson et al, because it would provide useful analytical data about the analytes. It would be well within the abilities of one having ordinary skill in the

art to use the channel structure shown by Simpson et al with any known prior art capillary electrophoretic technique, such as those claimed here.

Additionally, electroosmotic force corresponds to a type of pressure driving a fluid through a capillary, and as such, is considered a form of pressure-driven chromatography.

11. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al and Howitz et al as applied to claim 36 above, and further in view of Sundberg et al.

Simpson et al and Howitz et al disclose a combination as described above in addressing claim 36. Simpson et al and Arnold et al also disclose a combination as described above in addressing claim 36.

None among Simpson et al, Howitz et al, and Arnold et al disclose a parallel loading device comprising a pin for carrying and introducing the droplet of a liquid sample to the fluid interface port by contacting the virtual wall.

Sundberg et al disclose a parallel loading device (Figure 2) comprising a pin (38) for carrying and introducing the droplet of a liquid sample (36) to the ports (34) of a microfluidic system.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of either Simpson et al and Howitz et al or Simpson et al and Arnold et al by providing a parallel loading device comprising pins for carrying liquid samples to the fluid interface port, as taught by Sundberg et al,

because it would simplify delivery of small droplets. It would be well within the abilities of one having ordinary skill in the art to choose any known means of delivering fluid droplets to a selected spot in a microfluidic device (i.e. the port), such as that taught by Sundberg et al. A technique that delivers a plurality of droplets simultaneously, such as that of Sundberg et al, would be particularly obvious to choose, because it would aid in increasing throughput, decreasing labor, etc.

12. Claims 1-3, 5-8, 12-24, 26, 30-37, and 38-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al in view of Heller et al. (WO 99/64850) and either McCormick et al or Amigo. Since WO 99/64850 is in German, citations below are given to US Patent No. 6,846,398, which issued from the National Stage entry of this International Application.

The disclosure of Simpson et al is as described above in paragraph 9.

Heller et al disclose a device (Figures 1 and 2) comprising: fluid interface ports (A) formed in the side wall of a fluid channel to provide access to the interior of the fluid channel, wherein a separation medium is disposed in the interior of the fluid channel. (Column 5, lines 66-67) Relevant to claim 6, they also disclose a fluid interface port comprising an array of apertures. (Figures 1 and 2)

Relevant to claim 37, Heller et al disclose sample introduction via droplets on pins that guide the droplets to the interface port. (Column 6, lines 20-22)

Relevant to claim 39, Heller et al disclose a method of sample injection comprising: forming a droplet from the liquid sample, and directing the droplet to an

interface formed by a liquid in a fluid interface port formed in the side wall of a flow channel. (Column 6, lines 18-33)

Relevant to claims 40-45, they also disclose a method of forming their fluid interface ports, comprising the step of forming fluid interface ports in the channel sidewalls with diameter matched to the channel width, which can be 10-hundreds of microns. (Figures 1 and 2; Column 5, line 66 - Column 6, line 2; the formation of the cover inherently involves this step)

Heller et al do not explicitly disclose the thickness of the cover used in preparing their interface ports.

McCormick et al disclose a microfluidic system similar in construction to that of Heller et al, in which they cover the channels with a cover as thin as 10 microns. (Column 13, lines 17-22)

Amigo discloses a microfluidic system similar in construction to that of Heller et al, in which they cover the channels with a cover as thin as 10 microns. (Column 8, lines 1-6)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Simpson et al by replacing the sample and waste reservoirs, and their associated side channels with a simple hole or holes through the sidewall to serve as a fluid port, as taught by Heller et al, because Heller et al teach the that their fluid interface port increases the channel density attainable on microfluidic

chips, and reduces sample consumption. (Column 2, lines 19-64) The benefits in efficiency and throughput would have been obvious and highly desirable to a skilled artisan. It would also reduce the number of holes required in the device by eliminating the need for sample and waste reservoirs, this reduction in the number of holes having been taught by Simpson et al to be desirable. (Column 3, lines 50-65)

It would also have been obvious to one having ordinary skill in the art to specifically use a thin cover plate, such as those taught by either McCormick et al or Amigo, because the silence of Heller et al concerning cover thickness suitable for forming the interface port indicates that a skilled artisan could choose any suitable cover thickness such as those known in the prior art, e.g. McCormick et al or Amigo. The choice of thinner material could be motivated by reduction of material consumption, which could potentially reduce manufacturing costs. For a conventional channel that has a width of tens to hundreds of microns, this would meet the limitation to a port that is wider than it is deep.

Regarding the limitations to a "virtual wall" and port dead volume of less than a picoliter or zero, whether the separation medium forms a meniscus at the interior or exterior surface of the port depends on the cross-sectional area of the port vs. that of the channel - fluid will naturally be drawn into the narrower opening, driven by its surface tension. Conventional HF glass etching is used by Simpson et al, which results in a channel that is approximately twice as wide as it is deep. (Column 4, lines 47-67) An approximately hemicylindrical 60 micron wide, 30 micron deep channel would have a cross section of 450π square microns, while the port configuration of Figure 2 of Heller

et al for this channel would be a circle with 60 micron diameter, having a cross section twice as large. In the absence of applied pressure, fluid in the channel would not be drawn into the port to a significant extent, and the meniscus would form at the bottom surface of the wall, leading to a port dead volume of substantially zero. Given a conventional flowable separation medium, this meniscus could only correspond to the instantly claimed "virtual wall", as no distinction between the respective ports, associated channels, or fluids can be seen.

Further addressing claim 20, by replacing each sample reservoir with a fluid interface port, and eliminating waste reservoirs, the number of holes in this combination device would be reduced to N+A+C, where N is the number of samples to be analyzed, A is the number of anode reservoirs, and C is the number of cathode reservoirs.

Regarding claim 37, it would have been obvious to one having ordinary skill in the art at the time the invention was made to introduce sample droplets to the interface port via pins that are guided to the ports, as taught by Heller et al, because it would provide a convenient means of transfer at a lower cost than a pipetting device.

Regarding claim 39, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Simpson et al by altering the injection step by: forming a droplet of the sample and directing it to the virtual wall formed at a fluid interface port by a liquid in the separation channel (in the combination device of Simpson et al and Heller et al described above), as taught by Heller et al, because it would reduce waste of the sample liquid.

Regarding claims 40-45, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Simpson et al by replacing the step of forming sample reservoirs and associated side channels with the formation of a simple hole or holes through the sidewall to serve as a fluid port, as taught by Heller et al, because Heller et al teach the that their fluid interface port increases the channel density attainable on microfluidic chips, and reduces sample consumption. (Column 2, lines 19-64) The benefits in efficiency and throughput would have been obvious and highly desirable to a skilled artisan.

Regarding claims 46-48, each of these claims fully encompasses claim 1 in that they only recite limitations that are present in claim 1, while removing various other limitations. The prior art as applied to claim 1 above therefore also renders these claims obvious, given their open language (i.e. "comprising").

Regarding claim 49, a meniscus that forms anywhere from the upper to lower surface of the interface port can be described as "coplanar" with the sidewall channel.

13. Claims 9-11 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al, Heller et al, and either McCormick et al or Amigo as applied to claims 1 and 12 above, and further in view of Bjornson et al.

The reasoning for this rejection parallels that given above in paragraph 10.

Response to Arguments

14. Applicant's arguments filed 16 June 2005 have been fully considered but they are not persuasive.

Regarding the limitation that the port be wider than it is deep, as stated above, although the example given by Howitz et al does not meet this limitation, Howitz et al disclose variation of the depth of the port. (i.e. length of the capillary; Column 2, lines 5-10 and 27-30) Choice of a shorter length such that this limitation is met would have been obvious to a skilled artisan, particularly given the trend towards miniaturization in this art.

The newly added grounds for rejection also meet this limitation, as described above.

Regarding Applicant's contention that the Examiner has not provided an adequate and objective reason for combining the references, and that Simpson et al teach away from the combination, the Examiner considers the motivations provided in the rejections given above to meet the requirements of 35 U.S.C. §103(a). The cited portion of Simpson et al (Column 3, lines 12-21) in no way teaches away from this modification, and the Examiner maintains that it would have been well within the abilities of a skilled artisan to choose other means of sample introduction in the system of Simpson et al, given a proper motivation, which the Examiner considers to be present in the prior art and in the knowledge of one having ordinary skill in the art, as presented in the rejections above.

Conclusion

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Yager et al disclose fluid interface ports that could also read on the instantly claimed ports.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
11 October 2005

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